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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/083,476	02/27/2002	Roger N. Piasio	ISA-102.01	4777
63767	7590	03/05/2009	EXAMINER	
FOLEY HOAG, LLP			DEVI, SARVAMANGALA J N	
PATENT GROUP (w/ISA)				
155 SEAPORT BLVD.			ART UNIT	
BOSTON, MA 02210-2600			PAPER NUMBER	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary**Application No.**

10/083,476

Applicant(s)

PIASIO ET AL.

Examiner

S. Devi, Ph.D.

Art Unit

1645

Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12/05/08.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 22 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 22 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/55/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

Request for Continued Examination

1) A request for continued examination under 37 C.F.R. 1.114, including the fee set forth in 37 C.F.R. 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 C.F.R. 1.114, and the fee set forth in 37 C.F.R. 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 C.F.R. 1.114. Applicants' submission filed on 12/05/08 has been entered.

Applicants' Amendment

2) Acknowledgment is made of Applicants' amendment filed 12/05/08 in response to the final Office Action mailed 08/20/08.

Status of Claim(s)

3) Claim 22 has been amended via the amendment filed 12/05/08.
Claim is 22 is pending.

Prior Citation of Title 35 Sections

4) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

5) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Objection(s) Withdrawn

6) The objection to the specification made in paragraph 3 of the Office Action mailed 7/27/04 and maintained in paragraph 8 of the Office Action mailed 12/29/05, paragraph 6 of the Office Action mailed 12/05/06, paragraph 8 of the Office Action mailed 08/27/07, paragraph 7 of the Office Action mailed 01/24/08, and paragraph 5 of the Office Action mailed 08/20/08, is withdrawn.

Rejection(s) Withdrawn

- 7) The rejection of claim 22 made in paragraph 11 of the Office Action mailed 01/24/08 and maintained in paragraph 6 of the Office Action mailed 08/20/08 under 35 U.S.C. § 112, first paragraph, as containing new matter, is withdrawn in light of Applicants' amendment to the claim.
- 8) The rejection of claim 22 made in paragraph 10 of the Office Action mailed 08/20/08 under 35 U.S.C. § 112, first paragraph, as containing new matter, is withdrawn in light of Applicants' amendment to the claim.
- 9) The rejection of claim 22 made in paragraph 12(a) of the Office Action mailed 08/20/08 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.
- 10) The rejection of claim 22 made in paragraph 12(b) of the Office Action mailed 08/20/08 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

Rejection(s) under 35 U.S.C § 112, First Paragraph (Written Description)

- 11) Claim 22, as amended, is rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claim 22, as amended, is drawn to a method for detecting a symptomatic *Streptococcus pneumoniae* infection in a human subject of age 12 years or less comprising
The specification intends a detection method that maintains test specificity at 90% or better, that increases sensitivity of the test to urine samples from children with pneumococcal disease and that eliminates or at least minimizes false positives due to nasopharyngeal pneumococcal colonization. See paragraph bridging pages 16 and 17 of the instant specification. The *Written Description Guidelines* state:

There is an inverse correlation between the level of predictability in the art and the amount of disclosure necessary to satisfy the written description requirement. For example, if there is a well-established correlation between the structure and function in the art, one skilled in the art will be able to reasonably predict the complete structure of the claimed invention from its function.

However, from a review of the instant specification, it does not appear that at the time of the invention, Applicants had possession of a detection method that used one or more scrub lines positioned prior to a capture line in the sample flow path, which method yielded a test specificity of 90% or better, increased sensitivity to urine samples from children infected with pneumococci, and false positives due to nasopharyngeal pneumococcal colonization eliminated or minimized. For example, the method described in Example 3 of the instant specification is said to reduce conjugate concentration, reduce capture line concentration, and add one scrub line, whereas the method described in Example 4 is said to reduce conjugate concentration, reduce capture line concentration, and add two or three scrub lines. Table III depicts that when one scrub line was used with a scrub line antibody concentration of 0.3 to 0.6 mg/ml, 50% to 87.5% of the infected urine samples were positive, while 28% to 46% of the urine samples from nasopharyngeal carriers were also positive, i.e., false positive. Example 3 concludes that: (a) while these tests generally showed increasing elimination of false positives with increasing concentration of the scrub line, 'the specificity of the test was *adversely affected*'; and (b) increasing the concentration of the scrub line 'did *not* remove all antigen from the false positive samples' and it was therefore decided to try multiple scrub lines, each of lower concentration than the 0.3 mg/ml scrub line in one series of tests in that Example. Table IV depicts the results from Example 4. Although the use of 3 scrub lines at an antibody concentration of 0.1 mg/ml at each scrub line was effective in wholly eliminating false positives, it also *eliminated 80% of the positive samples*. The results from Table IV shows that the use of 2 scrub lines at antibody concentration of 0.1 mg/ml or above 0.1 mg/ml, i.e., 0.15, 0.2 and 0.25 mg/ml, '*adversely affected the test results on positive samples, decreasing specificity and sensitivity*'. Thus, the methods of detection that used one scrub line, or 2-3 scrub lines at various antibody concentrations did not accomplish the very objective of the instant invention, i.e., maintaining test specificity at 90% or better and increasing sensitivity of the test to children infected with pneumococci while eliminating or at least minimizing false positives due to nasopharyngeal pneumococcal colonization. The instant specification in the third full paragraph under Example 4 conveys Applicants' *intention to run further tests* using two or three scrub lines at lower concentrations than were incorporated in the series therein, 'to *try to eliminate* false positives without adversely affecting the sensitivity and specificity of the test' toward infected patient's

samples. Applicants again intend herein to 'try' combinations of 1-3 scrub lines with the capture line concentration and the optical density maintained at the level currently used for the NOW test on the premise that scrubbing out the level of antigen in the urine sample of most carriers prior to the capture line in both carrier and positive samples 'may' leave a sufficient antigen level in the urines of diseased patients to be detected at capture line of higher antibody concentration. This part of the specification states that it is important to recognize the *lack of any statistically significant figures* showing the level of antigen in the urine of healthy children nasopharyngeally colonized with *Streptococcus pneumoniae* and identifies the necessity for establishing how to screen healthy carriers of pneumococci and children actually having pneumococcal diseases. The specification herein makes the following statements that are indicative of Applicants' future plans and the current belief of what steps might work in a method that is intended to obtain test specificity of 90% or better and increased sensitivity to samples from pneumococcus-infected children with the false positives due to nasopharyngeal pneumococcal colonization eliminated or minimized (see page 16):

The medically recognized dangers in medicating otherwise healthy carrier children with antibiotics based on false positive test results render it urgent that this work, empirical though it be, continue forward rapidly.

Further test series on urines from other populations of children including nasopharyngeal carriers **are planned** with variations in other test parameters.

Some of them, involving the introduction of at least one scrub line positioned prior to the capture line in the sample flow path of the test devices **are believed to be capable of** being combined with the present concentrations of antibodies on the capture line and in the conjugate that are used in the NOW test.

With Applicants' own disclosure stating how the tested numbers of scrub lines at the tested concentrations of antibodies adversely affected the test results on positive samples from pneumococcus-infected children and decreased specificity and sensitivity, and the above-identified Applicants' plan, belief, and speculations, one of skill in the art cannot ascertain that Applicants had possession of a detection method that achieved the intended test specificity of 90% or better and increased sensitivity to samples from pneumococcus-infected children with false positives due to nasopharyngeal pneumococcal colonization eliminated or minimized. *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1568 (Fed. Cir. 1997), cert. denied, 523 U.S. 1089, 118 S. Ct. 1548 (1980), holds that an adequate written description requires 'not a mere wish or plan for obtaining the claimed invention.' *Eli Lilly*, 119 F.3d

at 1566. *Vas-Cath Inc. V. Mathukar*, 19 USPQ2d 1111 states that Applicant ‘must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention, is for purposes of the ‘written description’ inquiry, whatever is now claimed.’ See page 1117. The specification does not ‘clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.’ See page 1116 of *Vas-Cath Inc. V. Mathukar*, 19 USPQ2d 1111. Applicants should also note that *Vas-Cath Inc. V. Mathukar*, 19 USPQ2d 1111 makes clear that the written description provision of 35 U.S.C § 112, first paragraph, is severable from its enablement provision. See page 1115. Regardless of the complexity or simplicity of the method, conception cannot be achieved until reduction to practice has occurred. Adequate written description requires more than a mere statement that it is a part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. The claims are viewed as not meeting the written description provision of 35 U.S.C § 112, first paragraph.

Rejection(s) under 35 U.S.C § 112, Second Paragraph

12) The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his/her invention.

13) Claim 22 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

(a) Claim 22, as amended, is vague in the limitation: ‘the antigen’ (see line 11). For the purpose of distinctly claiming the subject matter, it is suggested that Applicants replace the above-identified limitation with the limitation --the C-polysaccharide antigen--.

(b) Claim 22, as amended, is vague in the limitation: ‘conjugates’ (see line 12). For the purpose of distinctly claiming the subject matter, it is suggested that Applicants replace the above-identified limitation with the limitation --conjugates of the tagged purified antibodies and the C-polysaccharide antigen--.

(c) Claim 22, as amended, is vague and/or confusing in the limitation: ‘the mixture, including the conjugates,’. See` line 13. For the purpose of distinctly claiming the subject

matter, it is suggested that Applicants replace the above-identified limitation with the limitation -the mixture comprising the conjugates--.

(d) Claim 22, as amended, is vague and/or incorrect in the limitation: 'the scrub line antibodies immobilized'. See line 16. To be consistent with the claim language used in line 7 of the claim, it is suggested that Applicants replace the above-identified limitation with the limitation --the scrub line antibodies having been immobilized--.

(e) Analogous rejection and criticism apply to claim 22, as amended, with regard to the limitation 'the capture line antibodies immobilized' in line 21 of the claim.

(f) Claim 22, as amended, is vague and confusing in the limitations: 'the capture line antibodies specific for the conjugates immobilized in the capture line downstream of the at least one scrub line'. See lines 23 and 24. For the purpose of distinctly claiming the subject matter, it is suggested that Applicants replace the above-identified limitations with the limitations --the immobilized capture line antibodies specific for the conjugates--.

(g) Claim 22, as amended, is vague and indefinite in the limitations: 'scrub line antibodies specific for the conjugates' and 'capture line antibodies specific for the conjugates'. The metes and bounds of the limitations in the amended claim are not clear because how these antibodies differ from each other in terms of scope is unclear. Are these the same antibodies each with the specificity to the conjugates, but used in two different locations, i.e., in capture lines and in scrub lines?

Remarks

14) Claim 22 stands rejected.

15) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. The Fax number for submission of amendments, responses and/or papers is (571) 273-8300, which receives transmissions 24 hours a day and 7 days a week.

16) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.Mov>. Should you have questions on access to the Private PAA

system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (in USA or CANADA) or 571-272-1000.

17) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Robert Mondesi, can be reached on (571) 272-0956.

/S. Devi/
Primary Examiner
AU 1645

March, 2009